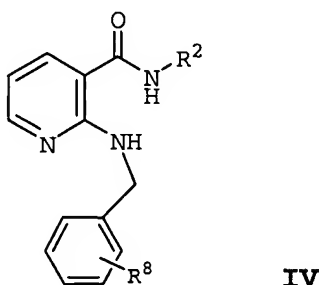


The listing of claims will replace all prior versions, and listings, of claims in the application:

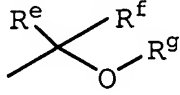
Listing of Claims

Claim 1 (currently amended): Compound of Formula IV



wherein R^2 is selected from unsubstituted or substituted phenyl, and 9-10 membered bicyclic and 11-14 membered tricyclic unsaturated or partially unsaturated heterocyclyl, wherein substituted R^2 is optionally substituted with one or more substituents selected from halo, C_{1-6} -alkyl, optionally substituted C_{3-6} -cycloalkyl, optionally substituted phenyl, optionally substituted phenyl- C_{1-4} -alkylenyl, C_{1-2} -haloalkoxy, optionally substituted phenyloxy, optionally substituted 4-6 membered heterocyclyl- C_{1-6} -alkyl, optionally substituted 4-6 membered heterocyclyl- C_{2-4} -alkenyl, optionally substituted 4-6 membered heterocyclyl, optionally substituted 4-6 membered heterocycliloxy, optionally substituted 4-6 membered heterocyclyl- C_{1-4} -alkoxy, optionally substituted 4-6 membered heterocyclylsulfonyl, optionally substituted 4-6 membered heterocyclylamino, optionally substituted 4-6 membered heterocyclylcarbonyl, optionally substituted 4-6 membered heterocyclyl- C_{1-4} -alkylcarbonyl, optionally substituted 4-6 membered heterocyclylcarbonyl- C_{1-4} -alkyl, optionally substituted 4-6 membered heterocyclyl- C_{1-4} -alkylcarbonylamino, optionally substituted 4-6 membered heterocyclyl-oxycarbonylamino, C_{1-2} -

haloalkyl, C₁₋₄-aminoalkyl, nitro, amino, C₁₋₃-alkylsulfonylamino, hydroxy, cyano, aminosulfonyl, C₁₋₂-alkylsulfonyl, halosulfonyl, C₁₋₄-alkylcarbonyl, amino-C₁₋₄-alkylcarbonyl, C₁₋₃-alkylamino-C₁₋₄-alkylcarbonyl, C₁₋₃-alkylamino-C₁₋₄-alkylcarbonylamino, C₁₋₄-alkoxycarbonyl-C₁₋₄-alkyl, C₁₋₃-alkylamino-C₁₋₃-alkyl, C₁₋₃-alkylamino-C₁₋₃-alkoxy, C₁₋₃-alkylamino-C₁₋₃-alkoxy-C₁₋₃-alkoxy, C₁₋₄-alkoxycarbonyl, C₁₋₄-alkoxycarbonylamino-C₁₋₄-alkyl, C₁₋₃-

alkylsulfonylamino-C₁₋₃-alkoxy, C₁₋₄-hydroxyalkyl,  and C₁₋₄-alkoxy;

wherein R^e and R^f are independently selected from H and C₁₋₂-haloalkyl; wherein R^g is selected from H, C₁₋₃-alkyl, optionally substituted phenyl-C₁₋₃-alkyl, 4-6 membered heterocyclyl, and optionally substituted 4-6 membered heterocyclyl-C₁₋₃-alkyl, C₁₋₃-alkoxy-C₁₋₂-alkyl and C₁₋₃-alkoxy-C₁₋₃-alkoxy-C₁₋₃-alkyl; and

wherein R⁸ is one or more substituents independently selected from halo, amino, nitro, hydroxy, C₁₋₆-alkyl, C₁₋₆-haloalkyl, C₁₋₆-alkoxy, C₁₋₆-haloalkoxy, C₁₋₆-aminoalkyl, C₁₋₆-hydroxyalkyl, optionally substituted phenyl, optionally substituted heterocyclyl, optionally substituted heterocyclyl-C₁₋₆-alkoxy, aminosulfonyl, C₃₋₆-cycloalkyl, C₁₋₆-alkylamino, C₁₋₆-alkylamino-C₁₋₆-alkyl, optionally substituted heterocyclyl-C₁₋₆-alkylamino, optionally substituted heterocyclyl-C₁₋₆-alkyl, C₁₋₆-alkylamino-C₂₋₄-alkynyl, C₁₋₆-alkylamino-C₁₋₆-alkoxy, C₁₋₆-alkylamino-C₁₋₆-alkoxy-C₁₋₆-alkoxy, and optionally substituted heterocyclyl-C₂₋₄-alkynyl;

and a pharmaceutically acceptable ~~isomers and derivatives~~ salt thereof;

provided R² is not 3-trifluoromethylphenyl when R⁸ is 4-hydroxy or 3-hydroxy.

Claim 2. (currently amended): Compound of Claim 1 wherein R² is selected from phenyl, 1,2-dihydroquinolyl, 1,2,3,4-tetrahydroisoquinolyl, 1',2'-dihydro-spiro[cyclopropane-1,3'-[3H]indol]-6'-yl, isoquinolyl, quinolyl, indolyl, isoindolyl, 2,3-dihydro-1H-indolyl, naphthyridinyl, 1,2,3,4-tetrahydro-[1,8]naphthyridinyl, dihydrobenzo[1,4]oxaxinyl, quinoxalinyl, benzo[d]isothiazolyl, 3,4-

dihydro-quinazolinyl, 2,3,4,4a,9,9a-hexahydro-1H-3-aza-fluorenyl,
 5,6,7-trihydro-1,2,4-triazolo[3,4-a]isoquinolyl, tetrahydroquinolyl,
 indazolyl, 2,1,3-benzothiadiazolyl, benzodioxanyl, benzothienyl,
 benzofuryl, benzimidazolyl, dihydro-benzimidazolyl, benzoxazolyl and
 benzthiazolyl, where R² is unsubstituted or substituted with one or
 more substituents selected from bromo, chloro, fluoro, iodo, nitro,
 amino, cyano, Boc-aminoethyl, hydroxy, oxo, fluorosulfonyl,
 methylsulfonyl, aminosulfonyl, 4-methylpiperazinylsulfonyl,
 cyclohexyl, phenyl, phenylmethyl, 4-pyridylmethyl, 4-
 morpholinylmethyl, 1-methylpiperazin-4-ylmethyl, 1-methylpiperazin-4-
 ylpropyl, morpholinylpropyl, piperidin-1-ylmethyl, 1-methylpiperidin-
 4-ylmethyl, 2-methyl-2-(1-methylpiperidin-4-yl)ethyl, 2-methyl-2-(4-
 pyrimidinyl)ethyl, 2-methyl-2-(5-methyloxadiazol-2-yl)ethyl, 2-methyl-
 2-(pyrazol-5-yl)ethyl, 2-methyl-2-(1-ethoxycarbonyl-1,2,3,6-
 tetrahydropyridin-4-yl)ethyl, morpholinylethyl, 1-(4-morpholinyl)-2,2-
 dimethylpropyl, 1-(4-morpholinyl)-2,2-dimethylethyl, piperidin-4-
 ylethyl, 1-Boc-piperidin-4-ylethyl, piperidin-1-ylethyl, 1-Boc-
 piperidin-4-ylethyl, piperidin-4-ylmethyl, 1-Boc-piperidin-4-ylmethyl,
 piperidin-4-ylpropyl, 1-Boc-piperidin-4-ylpropyl, piperidin-1-
 ylpropyl, pyrrolidin-1-ylpropyl, pyrrolidin-2-ylpropyl, 1-Boc-
 pyrrolidin-2-ylpropyl, 1-(pyrrolidin-1-yl)-2-methylpropyl, pyrrolidin-
 1-ylmethyl, pyrrolidin-2-ylmethyl, 1-Boc-pyrrolidin-2-ylmethyl, 2-
 methyl-2-(pyrrolidin-1-yl)ethyl, pyrrolidinylpropenyl,
 pyrrolidinylbutenyl, methylcarbonyl, Boc, piperidin-1-
 ylmethylcarbonyl, pyrrolidin-1-yl-carbonyl, pyrrolidin-2-yl-carbonyl,
 4-pyridylcarbonyl, 4-methylpiperazin-1-ylcarbonylethyl, CH₃O-C(=O)-CH₂-
 , methoxycarbonyl, aminomethylcarbonyl, dimethylaminomethylcarbonyl,
 methylsulfonylamino, dimethylaminomethylcarbonylamino, 1-pyrrolidinyl-
 CH₂-C(=O)-NH-, 4-morpholinyl-CH₂-C(=O)-NH-, 3-tetrahydrofuryl-O-C(=O)-
 NH-, cyclohexyl-N(CH₃)-, (4-pyrimidinyl)amino, (2-methylthio-4-
 pyrimidinyl)amino, 3-ethoxycarbonyl-2-methyl-fur-5-yl, 4-
 methylpiperazin-1-yl, 4-methyl-1-piperidyl, 1-Boc-4-piperidyl,
 piperidin-4-yl, 1-methylpiperidin-4-yl, 1-methyl-(1,2,3,6-
 tetrahydropyridyl), imidazolyl, morpholinyl, 4-trifluoromethyl-1-
 piperidinyl, hydroxybutyl, methyl, ethyl, propyl, isopropyl, butyl,
 tert-butyl, sec-butyl, trifluoromethyl, pentafluoroethyl,
 nonafluorobutyl, dimethylaminopropyl, 1,1-di(trifluoromethyl)-1-

hydroxymethyl, 1,1-di(trifluoromethyl)-1-(piperidinylethoxy)methyl, 1,1-di(trifluoromethyl)-1-(pyrrolidin-2-ylmethoxy)methyl, 1,1-di(trifluoromethyl)-1-(methoxyethoxyethoxy)methyl, 1-hydroxyethyl, 2-hydroxyethyl, trifluoromethoxy, 1-aminoethyl, 2-aminoethyl, 1-(N-isopropylamino)ethyl, 2-(N-isopropylamino)ethyl, 3-tetrahydrofuryloxy, dimethylaminoethoxy, 4-chlorophenoxy, phenyloxy, azetidin-3-ylmethoxy, 1-Boc-azetidin-3-ylmethoxy, 3-tetrahydrofurylmethoxy, pyrrolidin-2-ylmethoxy, 1-methylcarbonyl-pyrrolidin-2-ylmethoxy, 1-Boc-pyrrolidin-2-ylmethoxy, pyrrolidin-1-ylmethoxy, 1-methyl-pyrrolidin-2-ylmethoxy, 1-isopropyl-pyrrolidin-2-ylmethoxy, 1-Boc-piperdin-4-ylmethoxy, (1-pyrrolidinyl)ethoxy, piperdin-4-ylmethoxy, piperdin-3-ylmethoxy, 1-methylpiperdin-4-yloxy, methylsulfonylaminoethoxy, isopropoxy, methoxy and ethoxy; and a pharmaceutically acceptable ~~isomers and derivatives~~ salt thereof.

Claim 3 (currently amended): Compound of Claim 1 wherein R⁸ is one or more substituents independently selected from chloro, fluoro, bromo, hydroxy, methoxy, ethoxy, -O-CH₂-O-, trifluoromethoxy, 1-methylpiperidinylmethoxy, dimethylaminoethoxy, amino, dimethylamino, dimethylaminopropyl, diethylamino, aminosulfonyl, cyclohexyl, dimethylaminopropynyl, 3-(4-morpholinyl)propyn-1-yl, dimethylaminoethoxyethoxy, 3-(4-morpholinyl)propylamino, optionally substituted piperidinyl, morpholinyl, optionally substituted piperazinyl, optionally substituted phenyl, methyl, ethyl, propyl, cyano, hydroxymethyl, aminomethyl and trifluoromethyl;

and a pharmaceutically acceptable ~~derivatives~~ salt thereof.

Claim 4 (currently amended): Compound of Claim 2 wherein R² is selected from

- 1,2,3,4-tetrahydro-isoquinolyl optionally substituted with one or more substituents selected from methyl, and Boc,
- 1,2,3,4-tetrahydro-quinolyl optionally substituted with one or more substituents selected from methyl, Boc and oxo,
- 2,3-dihydro-1H-indolyl optionally substituted with one or more substituents selected from methyl, methylsulfonyl, 1-Boc-piperidin-4-ylmethyl, piperidin-4-ylmethyl, 1-Boc-piperidin-4-yl, piperidin-4-yl, 1-methyl-piperidin-4-ylmethyl, 1-methyl-

piperidin-4-yl, pyrrolidin-1-yl-carbonyl, dimethylaminomethylcarbonyl, aminomethylcarbonyl, methylcarbonyl, pyrrolidin-2-ylmethyl, and 1-Boc-pyrrolidin-2-ylmethyl, and 3,4-dihydro-2H-benzo[1,4]oxazinyl optionally substituted with one or more substituents selected from methyl, and methylcarbonyl; and a pharmaceutically acceptable derivatives-salt thereof.

Claim 5 (currently amended): Compound of Claim 4 wherein R² is 3,3-dimethyl-2,3-dihydro-1H-indolyl optionally substituted with a substituent selected from pyrrolidin-1-yl-carbonyl, methylcarbonyl, and methylsulfonyl; and a pharmaceutically acceptable derivatives-salt thereof.

Claim 6 (currently amended): Compound of Claim 4 wherein R² is 4,4-dimethyl-1,2,3,4-tetrahydro-1H-isoquinolinyl; and a pharmaceutically acceptable salt thereof.

Claim 7 (currently amended): Compound of Claim 3 wherein R⁸ is one or more substituents independently selected from fluoro, hydroxy, amino, and nitro; and a pharmaceutically acceptable derivatives-salt thereof.

Claim 8 (currently amended): Compound of Claim 3 wherein R⁸ is 4-fluoro; and a pharmaceutically acceptable derivatives-salt thereof.

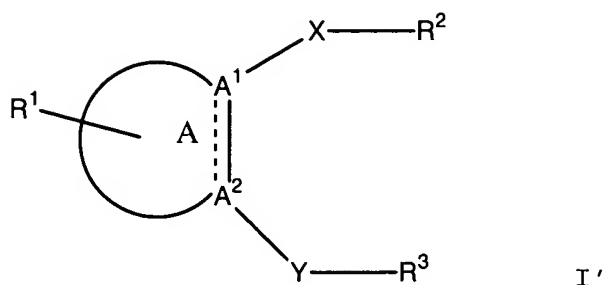
Claim 9 (currently amended): Compound of Claim 1 wherein R² is selected from phenyl substituted with one or more substituents selected from chloro, tert-butyl, azetidin-3-ylmethoxy, 1-Boc-azetidin-3-ylmethoxy, dimethylaminomethylcarbonylamino, 1,1-di(trifluoromethyl)-1-(pyrrolidin-2-ylmethoxy)methyl, trifluoromethyl, 2-methyl-2-(morpholin-4-yl)ethyl, 2-methyl-2-(pyrrolidin-1-yl)ethyl, 2-methyl-2-(5-methyloxadiazol-2-yl)ethyl, methylsulfonylamino, 1-methyl-pyrrolidin-2-ylmethoxy, and isopropyl; and a pharmaceutically acceptable derivatives-salt thereof.

10. (Original) A compound and pharmaceutically acceptable salts thereof selected from:

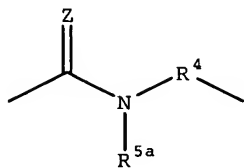
N-(3,3-Dimethyl-1-(methylsulfonyl)-2,3-dihydro-1H-indol-6-yl)-2-(((4-fluorophenyl)methyl)amino)-3-pyridinecarboxamide;
 N-(4-(1,1-dimethylethyl)-3-((N,N-dimethylglycyl)amino)phenyl)-2-(((4-fluorophenyl)methyl)amino)-3-pyridinecarboxamide;
 N-(3-(((2R)-1-methyl-2-pyrrolidinyl)methyl)oxy)-5-(trifluoromethyl)phenyl)-2-((3-(1,3-oxazol-5-yl)phenyl)amino)-3-pyridinecarboxamide;
 2-(((4-fluorophenyl)methyl)amino)-N-(3-(((2R)-1-methyl-2-pyrrolidinyl)methyl)oxy)-5-(trifluoromethyl)phenyl)-3-pyridinecarboxamide;
 2-(((4-fluorophenyl)methyl)amino)-N-(3-((methylsulfonyl)amino)-5-(trifluoromethyl)phenyl)-3-pyridinecarboxamide;
 2-((3-(1,3-oxazol-5-yl)phenyl)amino)-N-(3-(trifluoromethyl)phenyl)-3-pyridinecarboxamide;
 2-(((4-fluorophenyl)methyl)amino)-N-(4-(1-methyl-1-(5-methyl-1,3,4-oxadiazol-2-yl)ethyl)phenyl)-3-pyridinecarboxamide;
 3-(2-Chloro-5-([2-(4-fluoro-benzylamino)-pyridine-3-carbonyl]-amino)-phenoxy)methyl)-azetidine-1-carboxylic acid tert-butyl ester;
 N-[3-(Azetidin-3-ylmethoxy)-4-chloro-phenyl]-2-(4-fluoro-benzylamino)-nicotinamide;
 6-Chloro-3-(4-fluoro-benzylamino)-pyridazine-4-carboxylic acid (4-tert-butyl-phenyl)-amide;
 3-(4-Fluoro-benzylamino)-pyridazine-4-carboxylic acid (4-tert-butyl-phenyl)-amide;
 2-(4-Hydroxy-3-amino-benzylamino)-N-(4-isopropyl-phenyl)-nicotinamide;
 2-(4-Hydroxy-3-nitro-benzylamino)-N-(4-isopropyl-phenyl)-nicotinamide;
 3-(4-Fluoro-benzylamino)-1,2,5,6-tetrahydro-pyridazine-4-carboxylic acid (4-tert-butyl-phenyl)-amide; and
 N-[3-(Azetidin-3-ylmethoxy)-5-trifluoromethyl-phenyl]-2-(4-fluoro-benzylamino)-nicotinamide.

Claim 11 - 20. (Canceled).

Claim 21 (New): A compound of formula I'

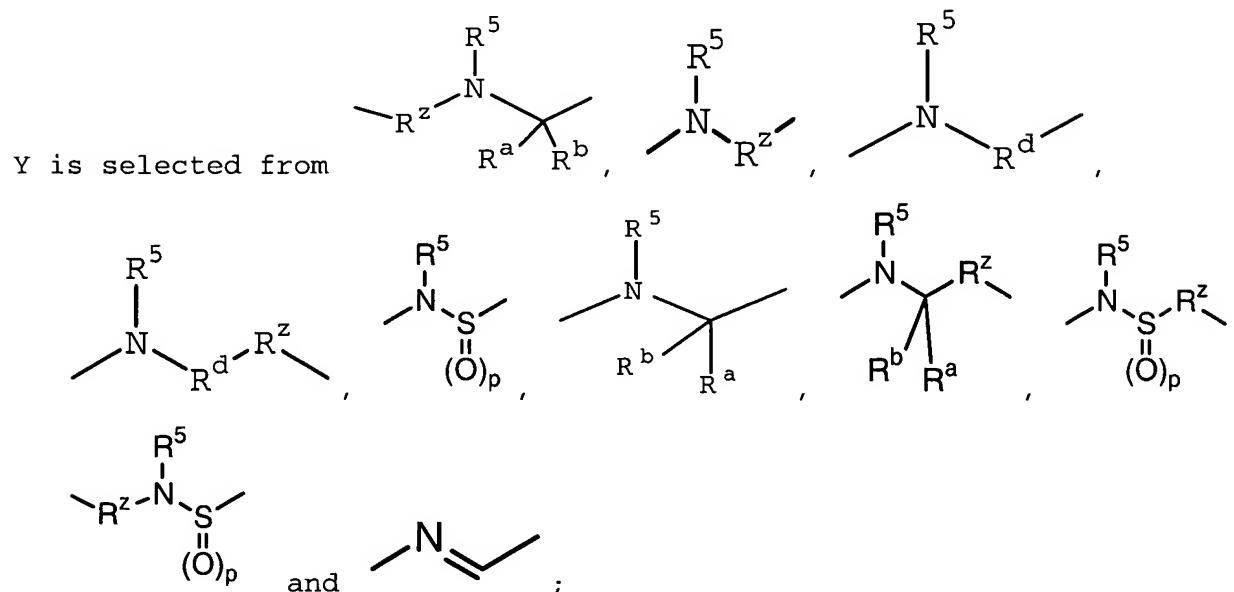


wherein each of A¹ and A² is independently C or N;
 wherein A¹-A² form part of a ring A selected from 5- or 6-membered heteroaryl;



wherein X is

wherein Z is oxygen or sulfur;



wherein p is 0 to 2,

wherein R^a and R^b are independently selected from H, halo, cyano, -NHR⁶ and C₁₋₄-alkyl substituted with R¹, or wherein R^a and R^b together form C₃-C₆ cycloalkyl;

wherein R^2 is selected from C_2-C_6 -alkylenyl, where one of the CH_2 groups may be replaced with an oxygen atom or an -NH-group; wherein one of the CH_2 groups may be substituted with one or two radicals selected from halo, cyano, $-NHR^6$ and C_{1-4} -alkyl substituted with R^1 ;

wherein R^d is cycloalkyl;

wherein R^1 is one or more substituents independently selected from H, halo, $-OR^7$, oxo, $-SR^7$, $-CO_2R^7$, $-COR^7$, $-CONR^7R^7$, $-NR^7R^7$, $-SO_2NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, optionally substituted cycloalkyl, optionally substituted phenylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted phenyl, lower alkyl, cyano, lower hydroxyalkyl, lower carboxyalkyl, nitro, lower alkenyl, lower alkynyl, lower aminoalkyl, lower alkylaminoalkyl and lower haloalkyl;

wherein R^2 is selected from

- a) substituted or unsubstituted 6-10 membered aryl,
- b) substituted or unsubstituted 5-6 membered heterocyclyl,
- c) substituted or unsubstituted 9-14 membered bicyclic or tricyclic heterocyclyl,
- d) cycloalkyl, and
- e) cycloalkenyl,

wherein substituted R^2 is substituted with one or more substituents independently selected from halo, $-OR^7$, oxo, $-SR^7$, $-CO_2R^7$, $-CONR^7R^7$, $-COR^7$, $-NR^7R^7$, $-NH(C_1-C_4 \text{ alkylenyl}R^9)$, $-SO_2R^7$, $-SO_2NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, $-NR^7C(O)NR^7R^7$, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted phenyl, halosulfonyl, cyano, alkylaminoalkoxy, alkylaminoalkoxyalkoxy, nitro, lower alkyl substituted with R^1 , lower alkenyl substituted with R^1 , and lower alkynyl substituted with R^1 ;

wherein R^3 is selected from aryl unsubstituted or substituted with one or more substituents independently selected from halo, $-OR^7$, $-SR^7$, $-SO_2R^7$, $-CO_2R^7$, $-CONR^7R^7$, $-COR^7$, $-NR^7R^7$, $-SO_2NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted phenyl, nitro, alkylaminoalkoxyalkoxy, cyano, alkylaminoalkoxy, lower alkyl substituted with R^1 , lower alkenyl substituted with R^1 , and lower alkynyl substituted with R^1 ;

wherein R^4 is selected from a direct bond, C_{2-4} -alkylenyl, C_{2-4} -alkenylenyl and C_{2-4} -alkynylenyl, where one of the CH_2 groups may be substituted with an oxygen atom or an $-NH-$, wherein R^4 is optionally substituted with hydroxy;

wherein R^5 is selected from H, lower alkyl, optionally substituted phenyl and lower aralkyl;

wherein R^{5a} is selected from H, lower alkyl, optionally substituted phenyl and lower aralkyl;

wherein R^6 is selected from H or C_{1-6} -alkyl; and

wherein R^7 is selected from H, lower alkyl, optionally substituted phenyl, optionally substituted heterocyclyl, optionally substituted C_3-C_6 -cycloalkyl, optionally substituted phenyl- C_{1-6} -alkyl, optionally substituted heterocyclyl- C_{1-6} -alkyl, optionally substituted C_3-C_6 cycloalkyl- C_{1-6} -alkyl, alkylaminoalkyl, and lower haloalkyl;

wherein R^9 is selected from H, optionally substituted phenyl, optionally substituted 5-6 membered heterocyclyl and optionally substituted C_3-C_6 cycloalkyl;

and a pharmaceutically acceptable salt thereof;

provided R^2 is not 3-trifluoromethylphenyl when A is pyridyl, when X is $-C(O)NH-$, when Y is $-NH-CH_2-$, when R^1 is H and R^3 is 3-(N-methylamino-carbonyl)phenyl, 4-hydroxyphenyl, 3-hydroxyphenyl or phenyl;

further provided R^2 is not substituted with $-SO_2NR^7R^7$ when Y is $-NHSO_2-$;

further provided R^2 is not 3-trifluoromethylphenyl when A is pyridyl, when X is $-C(O)NH-$, when Y is $-N(benzyl)-CH_2-$, when R^1 is H and when R^3 is phenyl;

further provided R^2 is not cyclohexyl when A is pyridyl, when X is $-C(O)NH-$, when Y is $-NH-CH_2-$, when R^1 is H and when R^3 is 2-methoxyphenyl or 3-methoxyphenyl;

further provided R^1 is not 2-hydroxymethylpyrrol-5-yl when A is pyridyl;

further provided R^1 is not 4-(methoxyaminocarbonylamino)phenyl when A is thienyl;

further provided R^1 is not 2-pyridylmethoxy when A is pyrimidyl, when X is $-C(O)NH-$, and when Y is $-NH-CH_2-$;

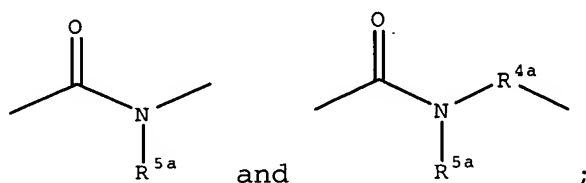
further provided R^1 is not 4-methylpiperidyl when A is pyrimidyl, when X is $-C(O)NH-$, when Y is $-NH-CH_2-$, and when R^3 is 3-chloro-4-methoxyphenyl;

further provided R^1 is not bromo when A is pyrimidyl, when X is $-C(O)NH-CH_2-$, when Y is $-NH-CH_2-$, and when R^3 is 3-chloro-4-methoxyphenyl;

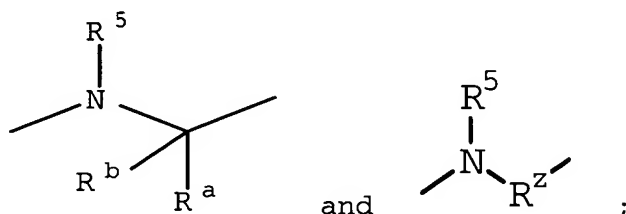
further provided R^2 is not 2-chloro-3-pyridyl when A is pyridyl; and

further provided R^2 is not 2-methoxyphenyl when A is pyridyl, when X is $-C(O)NH-$, when Y is $-NH-CH_2-$, when R^1 is H and R^3 is phenyl.

Claim 22 (New): Compound of Claim 21 wherein A is selected from thienyl, furanyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl, pyrazolyl, isoxazolyl, triazolyl, isothiazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl and triazinyl; wherein X is selected from



wherein Y is selected from



wherein R^a and R^b are independently selected from H, halo, and C_{1-2} -alkyl substituted with R^1 , or wherein R^a and R^b together form C_3-C_4 cycloalkyl;

wherein R^z is C_2-C_3 alkylene, where one of the CH_2 groups may be replaced with an oxygen atom or an $-NH-$;

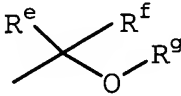
wherein R^1 is one or more substituents independently selected from H, halo, $-OR^7$, oxo, $-SR^7$, $-CO_2R^7$, $-CONR^7R^7$, $-COR^7$, $-NR^7R^7$, $-SO_2NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, optionally substituted C_{3-6} -cycloalkyl, optionally substituted phenyl- C_{1-4} -alkyl, optionally substituted 4-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted 4-6 membered heterocyclyl- C_{1-4} -alkyl, C_{1-6} -alkyl, cyano,

C₁₋₄-hydroxyalkyl, C₁₋₄-carboxyalkyl, nitro, C₂₋₃-alkenyl, C₂₋₃-alkynyl and C₁₋₄-haloalkyl;

wherein R² is selected from

substituted or unsubstituted aryl selected from phenyl, naphthyl, indanyl, indenyl and tetrahydronaphthyl, substituted or unsubstituted 5-6 membered heteroaryl, substituted or unsubstituted C₃₋₆-cycloalkyl and substituted or unsubstituted 9-10 membered bicyclic or 13-14

membered tricyclic saturated or partially unsaturated heterocyclyl wherein substituted R² is substituted with one or more substituents independently selected from halo, -OR⁷, oxo, -SR⁷, -SO₂R⁷, -CO₂R⁷, -CONR⁷R⁷, -COR⁷, -NR⁷R⁷, -NH(C₁-C₂-alkylenylR⁹), -(C₁-C₂-alkylenyl)NR⁷R⁷, -SO₂NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, C₁-C₆-alkylamino-C₁-C₆-alkoxy, C₁-C₆-alkylamino-C₁-C₆-alkoxy-C₁-C₆-alkoxy, halosulfonyl, optionally substituted 4-6 membered heterocyclyl-carbonylalkyl, C₁₋₄-

alkoxycarbonylamino-C₁₋₆-alkyl, , optionally substituted C₃₋₆-cycloalkyl, optionally substituted 4-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted phenyl-C₁₋₆-alkylenyl, optionally substituted 4-6 membered heterocyclyl-C₁-C₆-alkylenyl, 4-6 membered heterocyclyl-C₂-C₆-alkenylenyl, C₁₋₄-alkyl, cyano, C₁₋₄-hydroxyalkyl, nitro and C₁₋₄-haloalkyl;

wherein R³ is phenyl substituted with one or more substituents

independently selected from halo, -OR⁷, -SR⁷, -CO₂R⁷, -CONR⁷R⁷, -COR⁷, -NR⁷R⁷, -SO₂NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, C₃₋₆-cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, C₁₋₄-alkyl, C₁₋₄-aminoalkyl, cyano, C₁₋₄-hydroxyalkyl, nitro and C₁₋₄-haloalkyl;

wherein R^{4a} is C₂₋₄-alkylenyl where one of the CH₂ groups may be replaced with an oxygen atom or -NH-, wherein R^{4a} is optionally substituted with hydroxy;

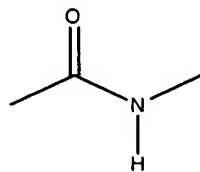
wherein R⁵ is selected from H and C₁-C₂-alkyl;

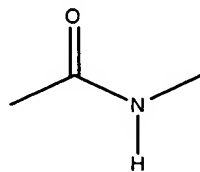
wherein R^{5a} is selected from H and C₁-C₂-alkyl; and

wherein R⁷ is selected from H, C₁₋₄-alkyl, optionally substituted phenyl, optionally substituted phenyl-C₁₋₄-alkyl, optionally substituted 4-6 membered heterocyclyl, optionally substituted 4-6

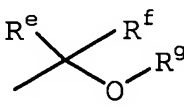
membered heterocyclyl-C₁₋₄-alkyl, optionally substituted C₃₋₆ cycloalkyl, C₁₋₂-alkylamino-C₁₋₄-alkyl and C₁₋₂-haloalkyl; wherein R^e and R^f are independently selected from H and C₁₋₂-haloalkyl; and wherein R^g is selected from H, C₁₋₆-alkyl, optionally substituted phenyl-C₁₋₆-alkyl, 4-6 membered heterocyclyl, optionally substituted 4-6 membered heterocyclyl-C₁₋₆-alkyl, C₁₋₄-alkoxy-C₁₋₄-alkyl and C₁₋₄-alkoxy-C₁₋₄-alkoxy-C₁₋₄-alkyl; and a pharmaceutically acceptable salt thereof.

Claim 23 (New): Compound of Claim 22 wherein A is selected from



pyridyl and pyrimidinyl; wherein X is ; wherein Y is -NH-CH₂-; wherein R¹ is one or more substituents independently selected from H, halo, hydroxy, C₁₋₂-alkoxy, C₁₋₂-haloalkoxy, amino, C₁₋₂-alkylamino, optionally substituted 5-6 membered heterocyclyl-C₁₋₂-alkylamino, aminosulfonyl, C₃₋₆-cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, C₁₋₄-alkyl, cyano, C₁₋₂-hydroxyalkyl, C₁₋₃-carboxyalkyl, nitro, C₂₋₃-alkenyl, C₂₋₃-alkynyl and C₁₋₂-haloalkyl; wherein R² is unsubstituted or substituted and selected from phenyl, naphthyl, indanyl, indenyl and tetrahydronaphthyl, substituted or unsubstituted 5-6 membered heteroaryl, C₃₋₆-cycloalkyl, and substituted or unsubstituted 9-10 membered bicyclic or 13-14 membered tricyclic heterocyclyl; wherein substituted R² is substituted with one or more substituents independently selected from halo, C₁₋₄-alkyl, optionally substituted C₃₋₆-cycloalkyl, optionally substituted phenyl, optionally substituted phenyl-C₁₋₄-alkylenyl, C₁₋₂-haloalkoxy, optionally substituted phenyloxy, optionally substituted 5-6 membered heterocyclyl-C₁₋₄-alkylenyl, optionally substituted 5-6 membered heterocyclyl-C₂₋₄-alkenylenyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted 5-6 membered heterocycliloxy, optionally substituted 5-6 membered heterocyclylsulfonyl, optionally substituted 5-6 membered heterocyclylamino, optionally substituted 5-6 membered heterocyclylcarbonyl, optionally substituted 5-6 membered heterocyclyl-C₁₋₄-alkylcarbonyl, C₁₋₂-haloalkyl, C₁₋₄-aminoalkyl, nitro,

amino, hydroxy, cyano, aminosulfonyl, C₁₋₂-alkylsulfonyl, halosulfonyl, C₁₋₄-alkylcarbonyl, C₁₋₃-alkylamino-C₁₋₃-alkyl, C₁₋₃-alkylamino-C₁₋₃-alkoxy, C₁₋₃-alkylamino-C₁₋₃-alkoxy-C₁₋₃-alkoxy, C₁₋₄-alkoxycarbonyl, C₁₋₄-

alkoxycarbonylamino-C₁₋₄-alkyl, C₁₋₄-hydroxyalkyl,  and C₁₋₄-alkoxy; wherein R³ is phenyl substituted with one or more substituents independently selected from halo, hydroxy, C₁₋₄-alkyl, C₁₋₂-alkoxy, optionally substituted 5-6 membered heterocyclyl-C₁₋₂-alkoxy, amino, C₁₋₂-alkylamino, aminosulfonyl, -NR³C(O)OR⁷, -NR³C(O)R⁷, C₃₋₆-cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, nitro, C₁₋₂-alkylamino-C₁₋₂-alkoxy-C₁₋₂-alkoxy, cyano, C₁₋₂-alkylamino-C₁₋₂-alkoxy, C₁₋₂-alkylamino-C₁₋₂-alkyl, C₁₋₂-alkylamino-C₂₋₃-alkynyl, C₁₋₂-hydroxyalkyl, C₁₋₂-aminoalkyl, C₁₋₂-haloalkyl, optionally substituted 5-6 membered heterocyclyl-C₂₋₃-alkenyl, and optionally substituted 5-6 membered heterocyclyl-C₂₋₃-alkynyl; and wherein R⁷ is selected from H, methyl, phenyl, cyclopropyl, cyclohexyl, benzyl, morpholinylmethyl, 4-methylpiperazinylmethyl, 4-methylpiperidinylmethyl, 4-morpholinylmethyl, 4-morpholinylethyl, 1-(4-morpholinyl)-2,2-dimethylpropyl, 1-piperidinylethyl, 1-piperidinylpropyl, 1-pyrrolidinylpropyl and trifluoromethyl; wherein R^e and R^f are independently -CF₃; and wherein R^g is selected from H, C₁₋₃-alkyl, optionally substituted phenyl-C₁₋₃-alkyl, optionally substituted 5-6 membered heterocyclyl-C₁₋₃-alkyl, C₁₋₃-alkoxy-C₁₋₃-alkyl and C₁₋₃-alkoxy-C₁₋₃-alkoxy-C₁₋₃-alkyl; and a pharmaceutically acceptable salt thereof.

Claim 24 (New): Compound of Claim 23 wherein A is pyridyl; wherein R¹ is one or more substituents independently selected from H, chloro, and fluoro; wherein R² is selected from phenyl, tetrahydronaphthyl, indanyl, naphthyl, imidazolyl, oxazolyl, furyl, pyrrolyl, isoxazolyl, pyrazolyl, thiazolyl, thiadiazolyl, thienyl, pyridyl, pyrimidinyl, pyridazinyl, cyclohexyl, 1,2-dihydroquinolyl, 1,2,3,4-tetrahydro-isoquinolyl, 1,2,3,4-tetrahydro-quinolyl, 2,3-dihydro-1H-indolyl, 2,3,4,4a,9,9a-hexahydro-1H-3-aza-fluorenyl, 5,6,7-trihydro-1,2,4-triazolo[3,4-a]isoquinolyl, 3,4-dihydro-2H-benzo[1,4]oxazinyl, and benzo[1,4]dioxanyl; wherein substituted R² is

substituted with one or more substituents independently selected from bromo, chloro, fluoro, iodo, nitro, amino, cyano, aminoethyl, Boc-aminoethyl, hydroxy, aminosulfonyl, 4-methylpiperazinylsulfonyl, cyclohexyl, phenyl, phenylmethyl, morpholinylmethyl, methylpiperazinylmethyl, morpholinylethyl, methylpiperazinylpropyl, 1-(4-morpholinyl)-2,2-dimethylpropyl, piperidinylmethyl, morpholinylpropyl, methylpiperidinylmethyl, piperidinylethyl, piperidinylpropyl, pyrrolidinylpropyl, pyrrolidinylpropenyl, pyrrolidinylbutenyl, fluorosulfonyl, methylsulfonyl, methylcarbonyl, piperidinylmethylcarbonyl, methylpiperazinylcarbonylethyl, methoxycarbonyl, 3-ethoxycarbonyl-2-methyl-fur-5-yl, methylpiperazinyl, methylpiperidyl, 1-methyl-(1,2,3,6-tetrahydropyridyl), imidazolyl, morpholinyl, 4-trifluoromethyl-1-piperidinyl, hydroxybutyl, methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, sec-butyl, trifluoromethyl, pentafluoroethyl, nonafluorobutyl, dimethylaminopropyl, 1,1-di(trifluoromethyl)-1-hydroxymethyl, trifluoromethoxy, 1,1-di(trifluoromethyl)-1-(piperidinylethoxy)methyl, 1,1-di(trifluoromethyl)-1-(methoxyethoxyethoxy)methyl, 1-hydroxyethyl, 2-hydroxyethyl, 1-aminoethyl, 2-aminoethyl, 1-(N-isopropylamino)ethyl, 2-(N-isopropylamino)ethyl, dimethylaminoethoxy, 4-chlorophenoxy, phenyloxy, 1-methylpiperidin-4-yloxy, isopropoxy, methoxy and ethoxy; and wherein R³ is phenyl substituted with one or more substituents selected from chloro, fluoro, bromo, hydroxy, methoxy, ethoxy, amino, dimethylamino, diethylamino, 1-methylpiperidinylmethoxy, aminosulfonyl, cyclohexyl, dimethylaminopropynyl, dimethylaminoethoxy, 3-(4-morpholinyl)propyn-1-yl, dimethylaminoethoxyethoxy, optionally substituted piperidinyl, morpholinyl, optionally substituted piperazinyl, optionally substituted phenyl, methyl, ethyl, propyl, cyano, hydroxymethyl, aminomethyl, nitro and trifluoromethyl; and a pharmaceutically acceptable salt thereof.

Claim 25 (New): Compound of Claim 21 and a pharmaceutically acceptable salt thereof selected from

N-(4-Chlorophenyl){3-[benzylamino](2-pyridyl)}carboxamide;

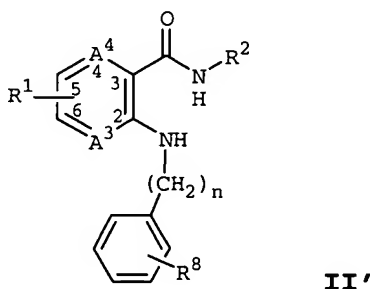
N-(4-Chlorophenyl) (3-{{(4-nitrophenyl)methyl}amino} (2-pyridyl)) -
 carboxamide;
 (2-{{(4-methoxyphenyl)methyl}amino} (2-pyridyl)) -N-(3-fluoro-4-
 methylphenyl) carboxamide;
 (6-Chloro-2-{{(4-methoxyphenyl)methyl}amino} (3-pyridyl)) -N-(3-fluoro-
 4-methylphenyl) carboxamide;
 (6-Chloro-2-{{(4-methoxyphenyl)methyl}amino} (3-pyridyl)) -N-(3-fluoro-
 4-methylphenyl) carboxamide ;
 (6-Chloro-2-{{(4-methoxyphenyl)methyl}amino} (3-pyridyl)) -N-(3-fluoro-
 4-methylphenyl) carboxamide, hydrochloride;
 (6-Chloro-2-{{(4-methoxyphenyl)methyl}amino} (3-pyridyl)) -N-(4-
 chlorophenyl) carboxamide;
 2-(3-Fluoro-benzylamino) -N-(4-phenoxy-phenyl) -nicotinamide;
 N-(4-Phenoxyphenyl) [2-{{[3-(trifluoromethyl)phenyl]methyl}amino} (3-
 pyridyl)] formamide;
 (2-{{(4-Fluorophenyl)methyl}amino} (3-pyridyl)) -N-(4-
 phenoxyphenyl) formamide;
 N-(4-Phenoxyphenyl) [2-{{[4-(trifluoromethyl)phenyl]methyl}amino} (3-
 pyridyl)] formamide;
 (2-{{(2-Bromophenyl)methyl}amino} (3-pyridyl)) -N-(4-
 phenoxyphenyl) formamide;
 N-(4-Phenoxyphenyl) [2-{{[4-(trifluoromethoxy)phenyl]methyl}amino} (3-
 pyridyl)] formamide;
 2-{{(2,3-Difluorophenyl)methyl}amino} (3-pyridyl)) -N-(4-
 phenoxyphenyl) formamide;
 N-(4-Chlorophenyl) (2-{{(4-cyanophenyl)methyl}amino} (3-
 pyridyl)) carboxamide;
 N-(4-Chlorophenyl) (2-{{(2-cyanophenyl)methyl}amino} (3-
 pyridyl)) carboxamide;
 N-(4-sec-butylphenyl) -2-[(4-fluorobenzyl) amino] nicotinamide;
 N-(4-tert-Butylphenyl) -2-[(4-fluorobenzyl) amino] nicotinamide;
 N-(4-Isopropyl-phenyl) -2-(3-methoxy-benzylamino) -nicotinamide;
 (2-{{(4-Fluorophenyl)methyl}amino} (3-pyridyl)) -N-[4-
 (methylethyl) phenyl] carboxamide;
 (2-{{(4-Fluorophenyl)methyl}amino} (3-pyridyl)) -N-[3-
 (trifluoromethyl) phenyl] carboxamide;

(2-[[(3,4-Dimethoxyphenyl)methyl]amino] (3-pyridyl)) -N- [3-(trifluoromethyl)phenyl]carboxamide;
 {2-[Benzylamino] (3-pyridyl)) -N- [3-(trifluoromethyl)phenyl]-carboxamide;
 (2-[[(3-Chlorophenyl)methyl]amino] (3-pyridyl)) -N- [3-(trifluoromethyl)phenyl]carboxamide;
 (2-[[(4-Bromophenyl)methyl]amino] (3-pyridyl)) -N- [3-(trifluoromethyl)phenyl]carboxamide;
 (2-[[(4-Chlorophenyl)methyl]amino] (3-pyridyl)) -N- [3-(trifluoromethyl)phenyl]carboxamide;
 (2-[[(2,4-Difluorophenyl)methyl]amino] (3-pyridyl)) -N- [3-(trifluoromethyl)phenyl]carboxamide;
 (2-[[(4-Fluorophenyl)ethyl]amino] (3-pyridyl)) -N- [3-(trifluoromethyl)phenyl]carboxamide;
 (2-[[(3,4-Difluorophenyl)methyl]amino] (3-pyridyl)) -N- [3-(trifluoromethyl)phenyl]carboxamide;
 (2-[[(2,3-Difluorophenyl)methyl]amino] (3-pyridyl)) -N- [3-(trifluoromethyl)phenyl]carboxamide;
 (2-[[(2-Fluorophenyl)methyl]amino] (3-pyridyl)) -N- [3-(trifluoromethyl)phenyl]carboxamide;
 (2-[[(2,6-Difluorophenyl)methyl]amino] (3-pyridyl)) -N- [3-(trifluoromethyl)phenyl]carboxamide;
 (2-[[(3-Bromophenyl)methyl]amino] (3-pyridyl)) -N- [3-(trifluoromethyl)phenyl]carboxamide;
 (2-[[(4-Fluorophenyl)methyl]amino] (3-pyridyl)) -N- [4-(trifluoromethyl)phenyl]carboxamide;
 N-[3-[3-(Dimethylamino)propyl]-5-(trifluoromethyl)phenyl] (2-[[(4-fluorophenyl)methyl]amino] (3-pyridyl)) carboxamide;
 {2-[(3-[3-(Dimethylamino)propyl]-4-fluorophenyl)methyl]amino] (3-pyridyl)) -N- [4-(tert-butyl)phenyl]carboxamide;
 {2-[(3-[3-(Dimethylamino)propyl]-4-fluorophenyl)methyl]amino] (3-pyridyl)) -N- [4-(trifluoromethyl)phenyl]carboxamide;
 {2-[(3-[3-(Dimethylamino)propyl]-4-fluorophenyl)methyl]amino] (3-pyridyl)) -N- (4-bromo-2-fluorophenyl)carboxamide;
 2-[(4-Fluorobenzyl)amino] -N- [4-tert-butyl-3-(1,2,3,6-tetrahydropyridin-4-yl)phenyl]nicotinamide;

[2-({[4-Fluoro-3-(3-morpholin-4-ylprop-1-ynyl)phenyl]methyl}amino)(3-pyridyl)]-N-[3-(trifluoromethyl)phenyl]carboxamide;
 {2-[(2H-Benzo[d]1,3-dioxol-5-ylmethyl)amino](3-pyridyl)]-N-(4-phenoxyphenyl)carboxamide;
 2-(4-Fluoro-benzylamino)-N-[3-(2-pyrrolidin-1-yl-ethoxy)-4-trifluoromethyl-phenyl]-nicotinamide;
 2-(4-Fluoro-benzylamino)-N-[3-(1-Boc-pyrrolidin-2-ylmethoxy)-4-pentafluoroethyl-phenyl]-nicotinamide;
 N-[4-tert-Butyl-3-(1-Boc-piperidin-4-ylmethoxy)-phenyl]-2-(4-fluoro-benzylamino)-nicotinamide;
 N-[3,3-Dimethyl-1-(1-methyl-piperidin-4-yl)-2,3-dihydro-1H-indol-6-yl]-2-(4-fluoro-benzylamino)-nicotinamide;
 N-[1-(2-Dimethylamino-acetyl)-3,3-dimethyl-2,3-dihydro-1H-indol-6-yl]-2-(4-fluoro-benzylamino)-nicotinamide;
 N-[1-(1-Boc-piperidin-4-yl)-3,3-dimethyl-2,3-dihydro-1H-indol-6-yl]-2-(4-fluoro-benzylamino)-nicotinamide;
 N-[3,3-Dimethyl-1-(2-Boc-amino-acetyl)-2,3-dihydro-1H-indol-6-yl]-2-(4-fluoro-benzylamino)-nicotinamide;
 2-(4-Fluoro-benzylamino)-N-(2-Boc-4,4-dimethyl-1,2,3,4-tetrahydro-isoquinolin-7-yl)-nicotinamide;
 N-[3-(1-Boc-pyrrolidin-2-ylmethoxy)-5-trifluoromethyl-phenyl]-2-(4-fluoro-benzylamino)-nicotinamide;
 N-[4-tert-Butyl-3-(1-Boc-pyrrolidin-2-ylmethoxy)-phenyl]-2-(4-fluoro-benzylamino)-nicotinamide;
 N-(4-Acetyl-2,2-dimethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-(4-fluoro-benzylamino)-nicotinamide;
 2-(4-Fluoro-benzylamino)-N-[3-(1-Boc-piperidin-4-ylmethoxy)-5-trifluoromethyl-phenyl]-nicotinamide.;
 2-(4-Fluoro-benzylamino)-N-[3-(pyrrolidin-2-ylmethoxy)-4-pentafluoroethyl-phenyl]-nicotinamide;
 2-(4-Fluoro-benzylamino)-N-[3-(pyrrolidin-2-ylmethoxy)-5-trifluoromethyl-phenyl]-nicotinamide;
 N-[4-tert-Butyl-3-(piperidin-4-ylmethoxy)-phenyl]-2-(4-fluoro-benzylamino)-nicotinamide;
 N-[4-tert-Butyl-3-(pyrrolidin-2-ylmethoxy)-phenyl]-2-(4-fluoro-benzylamino)-nicotinamide;

N-(4,4-Dimethyl-1,2,3,4-tetrahydro-isoquinolin-7-yl)-2-(4-fluoro-benzylamino)-nicotinamide;
 N-[1-(2-Amino-acetyl)-3,3-dimethyl-2,3-dihydro-1H-indol-6-yl]-2-(4-fluoro-benzylamino)-nicotinamide;
 N-(3,3-Dimethyl-1-piperidin-4-yl)-2,3-dihydro-1H-indol-6-yl)-2-(4-fluoro-benzylamino)-nicotinamide;
 2-(4-Fluoro-benzylamino)-N-[3-(piperidin-4-ylmethoxy)-5-trifluoromethyl-phenyl]-nicotinamide;
 N-(2,2-Dimethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-(4-fluoro-benzylamino)-nicotinamide;
 2-(4-Fluoro-benzylamino)-N-[3-(1-methyl-pyrrolidin-2-ylmethoxy)-5-trifluoromethyl-phenyl]-nicotinamide;
 N-[3,3-Dimethyl-1-(1-methyl-piperidin-4-ylmethyl)-2,3-dihydro-1H-indol-6-yl]-2-(4-fluoro-benzylamino)-nicotinamide;
 2-(4-Fluoro-benzylamino)-N-{4-[1-methyl-1-(1-methyl-piperidin-4-yl)-ethyl]-phenyl}-nicotinamide;
 N-(4,4-Dimethyl-2-oxo-1,2,3,4-tetrahydro-quinolin-7-yl)-2-(4-fluoro-benzylamino)-nicotinamide; and
 3-Benzo[1,3]dioxol-5-yl-3-[3-(4-pentafluoroethyl-phenylcarbamoyl)-pyridin-2-ylamino]-propionic acid.

Claim 26 (New): Compound of Claim 21 of formula II'



wherein each of A³ and A⁴ is independently CH or N, provided at least one of A³ and A⁴ is N;

wherein n is 1-2;

wherein R¹ is one or more substituents independently selected from H, chloro, fluoro, bromo, hydroxy, methoxy, ethoxy, trifluoromethoxy, oxo, amino, dimethylamino, aminosulfonyl, carboxymethyl, cyclopropyl, optionally substituted phenyl, methyl, ethyl, propyl,

cyano, hydroxymethyl, nitro, propenyl, propynyl, morpholinylethylamino, trifluoromethyl and unsubstituted or substituted heteroaryl selected from thienyl, furanyl, pyridyl, imidazolyl and pyrazolyl;

wherein R² is selected from a substituted or unsubstituted ring selected from phenyl, tetrahydronaphthyl, indanyl, benzodioxolyl, indenyl, naphthyl, isoxazolyl, pyrazolyl, thiazolyl, thiadiazolyl, thienyl, pyridyl, pyrimidinyl, pyridazinyl, 1,2-dihydroquinolyl, 1,2,3,4-tetrahydro-isoquinolyl, 1,2,3,4-tetrahydro-quinolyl, isoquinolyl, quinolyl, indolyl, isoindolyl, 2,3-dihydro-1H-indolyl, naphthyridinyl, quinoxalinyl, 2,3,4,4a,9,9a-hexahydro-1H-3-aza-fluorenyl, 5,6,7-trihydro-1,2,4-triazolo[3,4-a]isoquinolyl, indazolyl, 2,1,3-benzothiadiazolyl, 3,4-dihydro-2H-benzo[1,4]oxazinyl, benzodioxanyl, benzothienyl, benzofuryl, benzimidazolyl, benzoxazolyl and benzthiazolyl;

wherein substituted R² is substituted with one or more substituents independently selected from bromo, chloro, fluoro, iodo, nitro, amino, cyano, aminoethyl, Boc-aminoethyl, hydroxy, oxo, aminosulfonyl, 4-methylpiperazinylsulfonyl, cyclohexyl, phenyl, phenylmethyl, morpholinylmethyl, 1-methylpiperazin-4-ylmethyl, 1-methylpiperazin-4-ylpropyl, morpholinylpropyl, piperidin-1-ylmethyl, 1-methylpiperidin-4-ylmethyl, 2-methyl-2-(1-methylpiperidin-4-yl)ethyl, morpholinylethyl, 1-(4-morpholinyl)-2,2-dimethylpropyl, piperidin-4-ylethyl, 1-Boc-piperidin-4-ylethyl, piperidin-1-ylethyl, 1-Boc-piperidin-4-ylethyl, piperidin-4-ylmethyl, 1-Boc-piperidin-4-ylmethyl, piperidin-4-ylpropyl, 1-Boc-piperidin-4-ylpropyl, piperidin-1-ylpropyl, pyrrolidin-1-ylpropyl, pyrrolidin-2-ylpropyl, 1-Boc-pyrrolidin-2-ylpropyl, pyrrolidin-1-ylmethyl, pyrrolidin-2-ylmethyl, 1-Boc-pyrrolidin-2-ylmethyl, pyrrolidinylpropenyl, pyrrolidinylbutenyl, fluorosulfonyl, methylsulfonyl, methylcarbonyl, Boc, piperidin-1-ylmethylcarbonyl, 4-methylpiperazin-1-ylcarbonylethyl, methoxycarbonyl, aminomethylcarbonyl, dimethylaminomethylcarbonyl, 3-ethoxycarbonyl-2-methyl-fur-5-yl, 4-methylpiperazin-1-yl, 4-methyl-1-piperidyl, 1-Boc-4-piperidyl, piperidin-4-yl, 1-methylpiperidin-4-yl, 1-methyl-(1,2,3,6-tetrahydropyridyl),

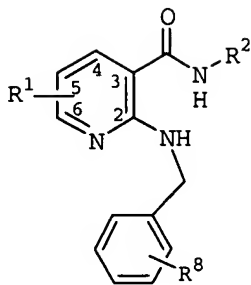
imidazolyl, morpholinyl, 4-trifluoromethyl-1-piperidinyl, hydroxybutyl, methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, sec-butyl, trifluoromethyl, pentafluoroethyl, nonafluorobutyl, dimethylaminopropyl, 1,1-di(trifluoromethyl)-1-hydroxymethyl, 1,1-di(trifluoromethyl)-1-(piperidinylethoxy)methyl, 1,1-di(trifluoromethyl)-1-(methoxyethoxyethoxy)methyl, 1-hydroxyethyl, 2-hydroxyethyl, trifluoromethoxy, 1-aminoethyl, 2-aminoethyl, 1-(N-isopropylamino)ethyl, 2-(N-isopropylamino)ethyl, dimethylaminoethoxy, 4-chlorophenoxy, phenyloxy, azetidin-3-ylmethoxy, 1-Boc-azetidin-3-ylmethoxy, pyrrol-2-ylmethoxy, 1-Boc-pyrrol-2-ylmethoxy, pyrrol-1-ylmethoxy, 1-methyl-pyrrol-2-ylmethoxy, 1-isopropyl-pyrrol-2-ylmethoxy, 1-Boc-piperidin-4-ylmethoxy, piperidin-4-ylmethoxy, 1-methylpiperidin-4-yloxy, isopropoxy, methoxy and ethoxy; and

wherein R^8 is one or more substituents independently selected from H, chloro, fluoro, bromo, hydroxy, methoxy, ethoxy, $-O-CH_2-O-$, trifluoromethoxy, 1-methylpiperidinylmethoxy, dimethylaminoethoxy, amino, dimethylamino, dimethylaminopropyl, diethylamino, aminosulfonyl, cyclohexyl, dimethylaminopropynyl, 3-(4-morpholinyl)propyn-1-yl, dimethylaminoethoxyethoxy, 3-(4-morpholinyl)propylamino, optionally substituted piperidinyl, morpholinyl, optionally substituted piperazinyl, optionally substituted phenyl, methyl, ethyl, propyl, cyano, hydroxymethyl, aminomethyl, nitro and trifluoromethyl;

and a pharmaceutically acceptable salt thereof;

provided R^2 is not 3-trifluoromethylphenyl when A^3 is N, when A^4 is CH, when n is 1, when R^1 is H and R^8 is 4-hydroxy, 3-hydroxy or H; further provided R^2 is not 2-chloro-3-pyridyl when A^3 is N, when A^4 is CH, when n is 1, when R^1 is H and R^8 is H or 4-methoxy; and further provided R^2 is not 2-methoxyphenyl when A^3 is N, when A^4 is CH, when n is 1, when R^1 is H and R^8 is H.

Claim 27 (New): Compound of Claim 21 of Formula III



III

wherein R¹ is one or more substituents independently selected from

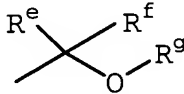
H,
halo,
hydroxy,
amino,
C₁₋₆-alkyl;
C₁₋₆-haloalkyl,
C₁₋₆-alkoxy,
C₁₋₂-alkylamino,
aminosulfonyl,
C₃₋₆-cycloalkyl,
cyano,
oxo,
C₁₋₂-hydroxyalkyl,
nitro,
C₂₋₃-alkenyl,
C₂₋₃-alkynyl,
C₁₋₆-haloalkoxy,
C₁₋₆-carboxyalkyl,
5-6-membered heterocyclyl-C₁₋₆-alkylamino,
unsubstituted or substituted phenyl and
unsubstituted or substituted 5-6 membered heterocyclyl;

wherein R² is selected from unsubstituted or substituted
phenyl, and

9-10 membered bicyclic and 13-14 membered tricyclic
unsaturated or partially unsaturated heterocyclyl,

wherein substituted R² is optionally substituted with one or more
substituents selected from halo, C₁₋₆-alkyl, optionally
substituted C₃₋₆-cycloalkyl, optionally substituted phenyl,

optionally substituted phenyl-C₁-C₄-alkyl, C₁₋₂-haloalkoxy, optionally substituted phenyloxy, optionally substituted 4-6 membered heterocyclyl-C₁-C₄-alkyl, optionally substituted 4-6 membered heterocyclyl-C₂-C₄-alkenyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted 4-6 membered heterocyclyloxy, optionally substituted 4-6 membered heterocyclyl-C₁-C₄-alkoxy, optionally substituted 5-6 membered heterocyclylsulfonyl, optionally substituted 5-6 membered heterocyclylamino, optionally substituted 5-6 membered heterocyclylcarbonyl, optionally substituted 5-6 membered heterocyclylcarbonyl-C₁₋₄-alkyl, optionally substituted 5-6 membered heterocyclyl-C₁₋₄-alkylcarbonyl, C₁₋₄-haloalkyl, C₁₋₄-aminoalkyl, nitro, amino, hydroxy, oxo, cyano, aminosulfonyl, C₁₋₂-alkylsulfonyl, halosulfonyl, C₁₋₄-alkylcarbonyl, amino-C₁₋₄-alkylcarbonyl, C₁₋₄-alkylamino-C₁₋₄-alkylcarbonyl, C₁₋₃-alkylamino-C₁₋₃-alkyl, C₁₋₃-alkylamino-C₁₋₃-alkoxy, C₁₋₃-alkylamino-C₁₋₃-alkoxy-C₁₋₃-alkoxy, C₁₋₄-alkoxycarbonyl, C₁₋₄-alkoxycarbonylamino-C₁₋₄-

alkyl, C₁₋₄-hydroxyalkyl,  and C₁₋₄-alkoxy;

wherein R^e and R^f are independently selected from H and C₁₋₂-haloalkyl;

wherein R⁷ is selected from H, C₁₋₃-alkyl, optionally substituted phenyl-C₁₋₃-alkyl, 4-6 membered heterocyclyl, and optionally substituted 4-6 membered heterocyclyl-C₁-C₃-alkyl;

wherein R^g is selected from H, C₁₋₃-alkyl, optionally substituted phenyl-C₁₋₃-alkyl, 4-6 membered heterocyclyl, and optionally substituted 4-6 membered heterocyclyl-C₁-C₃-alkyl, C₁₋₃-alkoxy-C₁₋₂-alkyl and C₁₋₃-alkoxy-C₁₋₃-alkoxy-C₁₋₃-alkyl; and

wherein R⁸ is one or more substituents independently selected from H, halo, amino, hydroxy, C₁₋₆-alkyl, C₁₋₆-haloalkyl, C₁₋₆-alkoxy, C₁₋₆-haloalkoxy, C₁₋₆-aminoalkyl, C₁₋₆-hydroxyalkyl, optionally substituted phenyl, optionally substituted heterocyclyl, optionally substituted heterocyclyl-C₁₋₆-alkoxy, aminosulfonyl, C₃₋₆-cycloalkyl, C₁₋₆-alkylamino, C₁₋₆-alkylamino-C₁₋₆-alkyl, optionally substituted heterocyclyl-C₁₋₆-alkylamino, optionally substituted heterocyclyl-C₁₋₆-alkyl, C₁₋₆-alkylamino-C₂₋₄-alkynyl, C₁₋₆-alkylamino-C₁₋₆-alkoxy, C₁₋₆-

alkylamino-C₁₋₆-alkoxy-C₁₋₆-alkoxy, and optionally substituted heterocyclyl-C₂₋₄-alkynyl;
 and a pharmaceutically acceptable salt thereof;
 provided R² is not 3-trifluoromethylphenyl when R¹ is H and R⁸ is 4-hydroxy, 3-hydroxy or H; and further provided R² is not 2-methoxyphenyl when R¹ is H and R⁸ is H.

Claim 28 (New): Compound of Claim 27 wherein R¹ is selected from H, chloro, fluoro, bromo, amino, hydroxy, methyl, ethyl, propyl, oxo, dimethylamino, aminosulfonyl, cyclopropyl, cyano, hydroxymethyl, nitro, propenyl, trifluoromethyl, methoxy, ethoxy, trifluoromethoxy, carboxymethyl, morpholinylethylamino, propynyl, unsubstituted or substituted phenyl and unsubstituted or substituted heteroaryl selected from thienyl,

furanyl, pyridyl, imidazolyl, and pyrazolyl;
 wherein R² is selected from phenyl, 1,2-dihydroquinolyl, 1,2,3,4-tetrahydro-isoquinolyl, 1,2,3,4-tetrahydro-quinolyl, 2,3-dihydro-1H-indolyl, 2,3,4,4a,9,9a-hexahydro-1H-3-aza-fluorenyl, 5,6,7-trihydro-1,2,4-triazolo[3,4-a]isoquinolyl, 3,4-dihydro-2H-benzo[1,4]oxazinyl, and benzo[1,4]dioxanyl, where R² is unsubstituted or substituted with one or more substituents selected from bromo, chloro, fluoro, iodo, nitro, amino, cyano, aminoethyl, Boc-aminoethyl, hydroxy, oxo, aminosulfonyl, 4-methylpiperazinylsulfonyl, cyclohexyl, phenyl, phenylmethyl, morpholinylmethyl, 1-methylpiperazin-4-ylmethyl, 1-methylpiperazin-4-ylpropyl, morpholinylpropyl, piperidin-1-ylmethyl, 1-methylpiperidin-4-ylmethyl, 2-methyl-2-(1-methylpiperidin-4-yl)ethyl, morpholinylethyl, 1-(4-morpholinyl)-2,2-dimethylpropyl, piperidin-4-ylethyl, 1-Boc-piperidin-4-ylethyl, piperidin-1-ylethyl, 1-Boc-piperidin-4-ylethyl, piperidin-4-ylmethyl, 1-Boc-piperidin-4-ylmethyl, piperidin-4-ylpropyl, 1-Boc-piperidin-4-ylpropyl, piperidin-1-ylpropyl, pyrrolidin-1-ylpropyl, pyrrolidin-2-ylpropyl, 1-Boc-pyrrolidin-2-ylpropyl, pyrrolidin-1-ylmethyl, pyrrolidin-2-ylmethyl, 1-Boc-pyrrolidin-2-ylmethyl, pyrrolidinylpropenyl, pyrrolidinylbutenyl, fluorosulfonyl, methylsulfonyl, methylcarbonyl, Boc, piperidin-1-ylmethylcarbonyl, 4-methylpiperazin-1-ylcarbonylethyl, methoxycarbonyl, aminomethylcarbonyl, dimethylaminomethylcarbonyl, 3-ethoxycarbonyl-2-methyl-fur-5-yl, 4-

methylnpiperazin-1-yl, 4-methyl-1-piperidyl, 1-Boc-4-piperidyl, piperidin-4-yl, 1-methylnpiperidin-4-yl, 1-methyl-(1,2,3,6-tetrahydropyridyl), imidazolyl, morpholinyl, 4-trifluoromethyl-1-piperidinyl, hydroxybutyl, methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, sec-butyl, trifluoromethyl, pentafluoroethyl, nonafluorobutyl, dimethylaminopropyl, 1,1-di(trifluoromethyl)-1-hydroxymethyl, 1,1-di(trifluoromethyl)-1-(piperidinylethoxy)methyl, 1,1-di(trifluoromethyl)-1-(methoxyethoxyethoxy)methyl, 1-hydroxyethyl, 2-hydroxyethyl, trifluoromethoxy, 1-aminoethyl, 2-aminoethyl, 1-(N-isopropylamino)ethyl, 2-(N-isopropylamino)ethyl, dimethylaminoethoxy, 4-chlorophenoxy, phenyloxy, azetidin-3-ylmethoxy, 1-Boc-azetidin-3-ylmethoxy, pyrrol-2-ylmethoxy, 1-Boc-pyrrol-2-ylmethoxy, pyrrol-1-ylmethoxy, 1-methyl-pyrrol-2-ylmethoxy, 1-Boc-piperidin-4-ylmethoxy, piperidin-4-ylmethoxy, 1-methylnpiperidin-4-yloxy, isopropoxy, methoxy and ethoxy; and

wherein R⁸ is one or more substituents independently selected from H, chloro, fluoro, bromo, hydroxy, methoxy, ethoxy, -O-CH₂-O-, trifluoromethoxy, 1-methylnpiperidinylmethoxy, dimethylaminoethoxy, amino, dimethylamino, dimethylaminopropyl, diethylamino, aminosulfonyl, cyclohexyl, dimethylaminopropynyl, 3-(4-morpholinyl)propyn-1-yl, dimethylaminoethoxyethoxy, 3-(4-morpholinyl)propylamino, optionally substituted piperidinyl, morpholinyl, optionally substituted piperazinyl, optionally substituted phenyl, methyl, ethyl, propyl, cyano, hydroxymethyl, aminomethyl and trifluoromethyl;

and a pharmaceutically acceptable salt thereof.

Claim 29 (New): Compound of Claim 28 wherein R¹ is selected from H, chloro or fluoro;

wherein R² is selected from

1,2,3,4-tetrahydro-isoquinolyl optionally substituted with one or more substituents selected from methyl, and Boc,

1,2,3,4-tetrahydro-quinolyl optionally substituted with one or more substituents selected from methyl, Boc and oxo,

2,3-dihydro-1H-indolyl optionally substituted with one or more substituents selected from methyl, 1-Boc-piperidin-4-ylmethyl, piperidin-4-ylmethyl, 1-Boc-piperidin-4-yl, piperidin-4-yl, 1-

methyl-piperidin-4-ylmethyl, 1-methyl-piperidin-4-yl, dimethylaminomethylcarbonyl, aminomethylcarbonyl, methylcarbonyl, pyrrolidin-2-ylmethyl, and 1-Boc-pyrrolidin-2-ylmethyl, and 3,4-dihydro-2H-benzo[1,4]oxazinyl optionally substituted with one or more substituents selected from methyl, and methylcarbonyl; and wherein R⁸ is one or more substituents independently selected from H, chloro, fluoro, bromo, cyano, methoxy, -O-CH₂-O-, amino, trifluoromethyl, trifluoromethoxy, 3-(4-morpholinyl)propyn-1-yl, dimethylaminopropyl, and 3-(4-morpholinyl)propylamino; and a pharmaceutically acceptable salt thereof.

Claim 30 (New): Compound of Claim 28 wherein R¹ is selected from H, chloro or fluoro; wherein R² is selected from phenyl optionally substituted with one or more substituents selected from bromo, chloro, fluoro, morpholinylmethyl, 1-methylpiperazin-4-ylmethyl, 1-methylpiperazin-4-ylpropyl, morpholinylpropyl, piperidin-1-ylmethyl, 1-methylpiperidin-4-ylmethyl, 2-methyl-2-(1-methylpiperidin-4-yl)ethyl, morpholinylethyl, 1-(4-morpholinyl)-2,2-dimethylpropyl, piperidin-4-ylethyl, 1-Boc-piperidin-4-ylethyl, piperidin-1-ylethyl, 1-Boc-piperidin-4-ylethyl, piperidin-4-ylmethyl, 1-Boc-piperidin-4-ylmethyl, piperidin-4-ylpropyl, 1-Boc-piperidin-4-ylpropyl, piperidin-1-ylpropyl, pyrrolidin-1-ylpropyl, pyrrolidin-2-ylpropyl, 1-Boc-pyrrolidin-2-ylpropyl, pyrrolidin-1-ylmethyl, pyrrolidin-2-ylmethyl, 1-Boc-pyrrolidin-2-ylmethyl, 4-methylpiperazin-1-yl, 4-methyl-1-piperidyl, 1-Boc-4-piperidyl, piperidin-4-yl, 1-methyl-(1,2,3,6-tetrahydropyridyl), methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, sec-butyl, trifluoromethyl, pentafluoroethyl, dimethylaminopropyl, dimethylaminoethoxy, 4-chlorophenoxy, phenyloxy, azetidin-3-ylmethoxy, 1-Boc-azetidin-3-ylmethoxy, pyrrol-1-ylethoxy, 1-methyl-pyrrol-2-ylmethoxy, pyrrol-2-ylmethoxy, 1-Boc-pyrrol-2-ylmethoxy, 1-Boc-piperdin-4-ylmethoxy, piperdin-4-ylmethoxy, and 1-methylpiperdin-4-yloxy; and wherein R⁸ is one or more substituents independently selected from H, chloro, fluoro, bromo, cyano, methoxy, -O-CH₂-O-, amino, trifluoromethyl, trifluoromethoxy, 3-(4-morpholinyl)propyn-1-yl, dimethylaminopropyl, and 3-(4-morpholinyl)propylamino;

and a pharmaceutically acceptable salt thereof.

Claim 31 (New): A pharmaceutical composition comprising a pharmaceutically-acceptable carrier and a compound as in Claim 1.

Claim 32 (New): A pharmaceutical composition comprising a pharmaceutically-acceptable carrier and a compound as in Claim 21.

Claim 33 (New): A method of treating cancer in a subject, said method comprising administering a therapeutically effective amount of a compound of Claim 1.

Claim 34 (New): A method of treating cancer in a subject, said method comprising administering a therapeutically effective amount of a compound of Claim 21.

Claim 35 (New): The method of Claim 33 comprising a combination with a compound selected from antibiotic-type agents, alkylating agents, antimetabolite agents, hormonal agents, immunological agents, interferon-type agents and miscellaneous agents.

Claim 36 (New): The method of Claim 34 comprising a combination with a compound selected from antibiotic-type agents, alkylating agents, antimetabolite agents, hormonal agents, immunological agents, interferon-type agents and miscellaneous agents.

Claim 37 (New): A method of treating angiogenesis in a subject, said method comprising administering a therapeutically effective amount of a compound of Claim 1.

Claim 38 (New): A method of treating angiogenesis in a subject, said method comprising administering a therapeutically effective amount of a compound of Claim 21.

Claim 39 (New): A method of treating proliferation-related disorders in a mammal, said method comprising administering a therapeutically effective amount of a compound of Claim 1.

Claim 40 (New): A method of treating proliferation-related disorders in a mammal, said method comprising administering a therapeutically effective amount of a compound of Claim 21.

Claim 41 (New): A method of reducing blood flow in a tumor in a mammal, said method comprising administering a therapeutically effective amount of a compound of Claim 1.

Claim 42 (New): A method of reducing blood flow in a tumor in a mammal, said method comprising administering a therapeutically effective amount of a compound of Claim 21.

Claim 43 (New): A method of reducing tumor size in a mammal, said method comprising administering a therapeutically effective amount of a compound of Claim 1.

Claim 44 (New): A method of reducing tumor size in a mammal, said method comprising administering a therapeutically effective amount of a compound of Claim 21.

Claim 45 (New): A method of treating diabetic retinopathy in a mammal, said method comprising administering a therapeutically effective amount of a compound of Claim 1.

Claim 46 (New): A method of treating diabetic retinopathy in a mammal, said method comprising administering a therapeutically effective amount of a compound of Claim 21.